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09/772,445	01/29/2001	Hynda K. Kleinman	2600-109	1045

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EXAMINER	
NIEBAUER, RONALD T	

ART UNIT	PAPER NUMBER
1654	

NOTIFICATION DATE	DELIVERY MODE
04/29/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PTO-PAT-Email@rfem.com

Office Action Summary	Application No.	Applicant(s)	
	09/772,445	KLEINMAN ET AL.	
	Examiner	Art Unit	
	RONALD T. NIEBAUER	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 February 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-40,53-61,133-136,173-176 and 178-186* is/are pending in the application.

4a) Of the above claim(s) *9,10,12,20,21,31,32,37,40,56 and 178-182* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,11,13-19,22-30,33-36,38,39,53-55,57-61,133-136,173-176 and 183-186* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9/17/08 has been entered.

Applicants amendments, arguments, and affidavit filed 9/17/08 are acknowledged and have been fully considered. Any rejection and/or objection not specifically addressed is herein withdrawn.

Previously, applicant elected group 1 (claims 1-40,47-49,53-61,133-136) (11/5/04) and elected a species comprising amino acids LKKTET (2/24/05) for the would healing polypeptide. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Due to the addition of new claims an additional election of species requirement was sent 1/6/09.

Applicant's election of the following species:

Patient population: skin wound

Further agent: transforming growth factor beta

Further excipient: sterile water

in the reply filed on 2/5/09 is acknowledged. Applicant states that claims 183-184 read on the elected species of wound healing polypeptide. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 41-52,62-132,137-172,177 have been cancelled.

Claims 178-182 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 11/5/04.

Claims 9-10,12,20-21,31-32,37,40,56 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 2/5/09.

In particular, claims 9-10,20-21 are to a species of wound healing polypeptide other than LKKTET. Claims 12,31-32,37 are to a species of further agent other than transforming growth factor beta. Claims 40,56 are to a patient population other than skin wound.

In the instant case, each of the elected species were found in the prior art. Any art that was found in the course of searching for the elected species that reads on non-elected species is also cited herein. In accord with section 803.02 of the MPEP the Markush-type claims and the claims to the elected species are rejected and claims to the nonelected species are held withdrawn from consideration.

Claims 1-8,11,13-19,22-30,33-36,38-39,53-55,57-61,133-136,173-176,183-186 are under consideration.

Claim Objections

Claims 1,23,136,185-186 are objected to because of the following informalities:

Claims 1,23,185-186 refer to TB4,TB4ala,TB9,TB10,TB11,TB12,TB13,TB14,TB15. The abbreviations should be identified the first time they are used in the claims. Also, consistent nomenclature (B vs beta as used in claims 1-2 for example) should be used throughout.

Claim 136 recites phophatidylcholine 2 times within the same group. As such one of the occurrences of phophatidylcholine can be deleted.

Claim 136 refers to 'ethyloeate'. It appears that there is a space missing between the word 'ethyl' and the word 'oleate'.

Appropriate correction is required.

Specification

The incorporation of essential material in the specification by reference to an unpublished U.S. application, foreign application or patent, or to a publication is improper. Applicant is required to amend the disclosure to include the material incorporated by reference, if the material is relied upon to overcome any objection, rejection, or other requirement imposed by the Office. The amendment must be accompanied by a statement executed by the applicant, or a practitioner representing the applicant, stating that the material being inserted is the material previously incorporated by reference and that the amendment contains no new matter. 37 CFR 1.57(f).

In the instant case, on page 9 of the specification applicants refer to isoforms of a Mihelic et al publication. It is noted that Mihelic et al is not a U.S. patent or U.S. patent application publication.

37 CFR 1.57(c) prohibits incorporation by reference to essential subject matter using an unpublished U.S. application, foreign application or patent, or to a publication. 37 CFR 1.57(c) recites:

(c) " **Essential material** " may be incorporated by reference, but **only by way of an incorporation by reference to a U.S. patent or U.S. patent application publication**, which patent or patent application publication does not itself incorporate such essential material by reference. "Essential material " is material that is necessary to:
(1) Provide a written description of the claimed invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and set forth the best mode contemplated by the inventor of carrying out the invention as required by the first paragraph of 35 U.S.C. 112;
(2) Describe the claimed invention in terms that particularly point out and distinctly claim the invention as required by the second paragraph of 35 U.S.C. 112; or
(3) Describe the structure, material, or acts that correspond to a claimed means or step for performing a specified function as required by the sixth paragraph of 35 U.S.C. 112."

The subject matter is "Essential material" since it provides written description as defined in sub paragraph (1) and (2). Since the "Essential material," claimed in the instant application, is not recited in a "U.S. patent or U.S. patent application publication, which patent or patent application publication does not itself incorporate such essential material by reference," it is improper to provide support via the "incorporation by reference" means. In the instant case, applicants attempts to incorporate Mihelic et al is improper.

The incorporation by reference will not be effective until correction is made to comply with 37 CFR 1.57(b), (c), or (d). If the incorporated material is relied upon to meet any outstanding objection, rejection, or other requirement imposed by the Office, the correction must

be made within any time period set by the Office for responding to the objection, rejection, or other requirement for the incorporation to be effective. Compliance will not be held in abeyance with respect to responding to the objection, rejection, or other requirement for the incorporation to be effective. In no case may the correction be made later than the close of prosecution as defined in 37 CFR 1.114(b), or abandonment of the application, whichever occurs earlier.

Any correction inserting material by amendment that was previously incorporated by reference must be accompanied by a statement that the material being inserted is the material incorporated by reference and the amendment contains no new matter. 37 CFR 1.57(f).

Priority

Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(e) as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed application, Application No. 60/094,690 (7/30/98), fails to provide adequate written description in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application.

In the instant case, Claims 1-8,11,13,16-18,22-30,33-36,38-39,53-55,57-61,133-136,173-176,183-186 refer to the amino acid sequence LKKTET or to isoforms.

Lack of Ipsis Verbis Support

Application No. 60/094,690 (7/30/98), is void of support for the amino acid sequence LKKTET or for isoforms.

Lack of Implicit or Inherent Support

Section 2163 of the MPEP states: 'While there is no in haec verba requirement, newly added claim limitations must be supported in the specification through express, implicit, or inherent disclosure'.

Although the above statement is with respect to new claim limitations, the analysis is similar in determining conditions for receiving the benefit of an earlier filing date.

Application No. 60/094,690 (7/30/98), does recite thymosin beta 4. However, the disclosure of thymosin beta 4 would not lead one to the sequence LKKTET or to isoforms. For at least these reasons, one would not conclude that Application No. 60/094,690 provides adequate support for Claims 1-8,11,13,16-18,22-30,33-36,38-39,53-55,57-61,133-136,173-176,183-186.

The disclosure of the prior-filed application, PCT/US99/17282 (7/29/99), fails to provide adequate written description in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application.

In the instant case, Claim 136 recites 'lactated Ringer's intravenous polyalklene glycol'. Claims 173-176 are drawn to ranges of at least about 0.01 ng/ml and up to about 60 ug per 300 microliter. Claims 185-186 are drawn to diseases including 'neuron-degenerative disease'.

Lack of Ipsis Verbis Support

PCT/US99/17282 is void of support for 'lactated Ringer's intravenous polyalklene glycol'. PCT/US99/17282 is void of support for 'at least about 0.01 ng/ml and up to about 60 ug per 300 microliter'. PCT/US99/17282 is void of support for the word 'neuron'.

Lack of Implicit or Inherent Support

Section 2163 of the MPEP states: 'While there is no in haec verba requirement, newly added claim limitations must be supported in the specification through express, implicit, or inherent disclosure'.

Although the above statement is with respect to new claim limitations, the analysis is similar in determining conditions for receiving the benefit of an earlier filing date.

PCT/US99/17282 refers to Ringer's intravenous vehicles. However, such disclosure does not lead one to 'lactated Ringer's intravenous polyalklene glycol' of claim 136.

PCT/US99/17282 (figures 6-7) shows specific concentrations of thymosin beta 4 used in a particular assay. However, there is no support for 'about' 0.01 ng/ml or 'about' 60 ug per 300 microliter. Further, it appears that disparate sections of the specification have been used to come up with the ranges recited in the claims. It is noted that claims 173-176 depend from claims 1,13,23,53 respectively. However, one would not have necessarily recognized the use of the instantly claimed ranges for applications of claims 1,13,23,53.

PCT/US99/17282 does not use the word 'neuron' thus one would recognize that 'neuron-degenerative disease' of claims 185-186 are not contemplated.

For at least these reasons, one would not conclude that PCT/US99/17282 provides adequate support for Claims 136,173-176,185-186.

It is noted that section 706.02 VI D of the MPEP sets forth the method to determine the effective filing date. In particular, 'If the application properly claims benefit under 35 U.S.C. 119(e) to a provisional application, the effective filing date is the filing date of the provisional application for any claims which are fully supported under the first paragraph of 35 U.S.C. 112 by the provisional application.'. It is noted that claims are either fully supported or not fully supported. In other words, claims are not treated as 'supported in part' even though one particular element may be supported in the provisional application. In the instant case, claims 14-15,19 are searched based on a priority date of 7/30/98. Claims 1-8,11,13,16-18,22-30,33-36,38-39,53-55,57-61,133-135 are searched based on a priority date of 7/29/99.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-8,11,13,22-30,33-36,38-39,53,61,133-136,173-176,183-186 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-2,13,23-24,53,185-186 and dependent claims refer to an isoform. Isoforms are discussed on pages 9-10 of the specification. However, no specific definition of isoform is set

forth. There is no standard art-recognized definition of isoform. For example, it is unclear what structural features or % homology is required for an isoform. Although the specification states that some isoforms have about 70% homology such information is not recited in the instant claims. It is noted that the specification refers to TB4 isoforms that have not yet been identified. However, the structural features of an isoform that has not been identified are unclear. There is more than one reasonable interpretation of what falls within the scope of the claims. As discussed above (see section 'specification') applicants attempt to incorporate by reference Mihelic et al is not proper.

Claims 1,23,185-186 refer to conservative variants. It is noted that the claims state that 'at least one of a hydrophobic amino acid residues is replaced for another hydrophobic amino acid residue in said amino acid sequence or a polar amino acid residue is replaced for another polar amino acid residue'. However, the claims are not limited to those changes (note the use of the phrase 'at least'). The specification (page 11) defines conservative variant to denote the replacement of an amino acid residue by another biologically similar residue. Further the specification states that changes include glutamine for asparagine 'and the like'. The term 'biologically similar' is a relative term which renders the claim indefinite. The term 'biologically similar' is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. In the instant case, it is unclear if biologically similar means similar in size, hydrophobicity, charge, or some other characteristic. Further the term 'and the like' is unclear since it is unclear in which way the changes are alike. There is more than one reasonable interpretation of what falls within the scope of the claims.

Claims 1-8,11,13,22-30,33-36,38-39,53,61,133-136,173-176,183-186 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him. The courts have stated:

> "To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997); In re Gostelli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966." Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In *Regents of the University of California v. Eli Lilly & Co.* the court stated:

> "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *Fiers*, 984 F.2d at 1171, 25 USPQ2d 1601; *In re Smythe*, 480 F.2d 1376, 1383, 178 USPQ 279, 284985 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus …") *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

The MPEP further states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence,

it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP § 2163. The MPEP does state that for a generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. MPEP § 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP § 2163. Although the MPEP does not define what constitute a sufficient number of representative species, the courts have indicated what do not constitute a representative number of species to adequately describe a broad generic. In *Gostelli*, the courts determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli*, 872, F.2d at 1012, 10 USPQ2d at 1618.

The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include "level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient." MPEP § 2163. While all of the factors have been considered, a sufficient amount for a *prima facie* case are discussed below.

In the instant case, the claims are drawn to methods comprising administering a polypeptide or a conservative variant or isoform having wound-healing activity.

(1) Level of skill and knowledge in the art:

The level of skill in the art is high with regard to methods of wound healing. The level of knowledge in the art is low regarding understanding the functional effects of varying a particular peptide sequence given that the effects of substitutions cannot be predicted a priori.

(2) Partial structure:

Although unclear (see 112 2nd) the terms 'isoform' and 'conservative variant' are given the broadest reasonable interpretation. It is noted that certain claims state that 'at least one of a hydrophobic amino acid residues is replaced for another hydrophobic amino acid residue in said amino acid sequence or a polar amino acid residue is replaced for another polar amino acid residue'. However, the claims are not limited to those changes (note the use of the phrase 'at least'). In considering the size of the genus it is noted that thymosin beta 4 is shown in figure 10a as having 43 residues. In considering isoforms with 70% homology (which is clearly within the genus as recited in the specification page 9), such isoforms of thymosin beta 4 can have substitutions at 12 positions for example. If there are 12 substitutions with any of the 20 naturally occurring amino acids there are at least 20^{12} (i.e. 4096000000000000) different compounds. The specification (figure 11a for example) provides examples of a few isoforms. However, the examples represent a small fraction of the possible variety of the genus. Further, there appears to be no specific examples of conservative variants.

Since there are a substantial variety of polypeptides possible within the genus, the limited examples do not constitute a representative number of species and do not sufficiently describe the genus claimed (see *Gostelli* above).

(3) Physical and/or chemical properties and (4) Functional characteristics:

The peptides and variants are recited as having wound-healing activity. There is no disclosed correlation between this functional characteristic and any structure. One of skill in the art would not recognize which variants are sufficient to have wound-healing activity and one could not a priori predict the properties. There are no common structural attributes that identify wound-healing peptides. As such, one of skill in the art would not recognize a core structure or common attributes of the wound-healing peptides. One of skill in the art would not recognize wound-healing peptides outside of those specifically identified. There is no teaching in the specification regarding what part of the structure can be varied while retaining the ability to be a wound-healing peptides. In particular, no common core sequence is taught. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus and that there is a lack of the knowledge in the art regarding which amino acids can vary to maintain the function and thus that the applicant was not in possession of the claimed genus.

(5) Method of making the claimed invention:

The specification does not seem to specifically set forth examples of making peptides of the instant invention. It appears that the examples are drawn to thymosin beta 4. However, such peptide is not representative of the instant genus nor does the peptide itself provide a specific correlation between structure and function such that one could identify any and all wound healing polypeptides.

As stated *supra*, the MPEP states that written description for a genus can be achieved by a representative number of species within a broad generic. It is unquestionable that claim(s) 1-

8,11,13,22-30,33-36,38-39,53,61,133-136,173-176,183-186 is/are broad and generic, with respect to all conservative variants encompassed by the claims. The possible structural variations are numerous to any variant. Although the claims may recite some functional characteristics, the claims lack written description because there is no disclosure of a correlation between function and structure of the compounds beyond those compounds specifically disclosed in the examples in the specification. Moreover, the specification lack sufficient variety of species to reflect this variance in the genus. While having written description peptides identified in the specification tables and/or examples, the specification does not provide sufficient descriptive support for the myriad of compounds embraced by the claims.

The description requirement of the patent statue requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736, F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.") Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

Response to Arguments written description

Since claims were previously rejected under 112 1st written description, applicants arguments will be considered to the extent that they apply to the instant rejections.

Applicants argue that the claims have been amended to recite specific replacements of the variants.

Applicant's arguments filed 9/17/08 have been fully considered but they are not persuasive.

Although Applicants argue that the claims have been amended to recite specific replacements of the variants, the claims are not limited to those variants. It is noted that the claims use the language 'at least'. As such one would recognize that the claims are open to other modifications, substitutions, and variations.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 136,173-176,185-186 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In the instant case, Claim 136 recites 'lactated Ringer's intravenous polyalklene glycol'. Claims 173-176 are drawn to ranges of at least about 0.01 ng/ml and up to about 60 ug per 300 microliter. Claims 185-186 are drawn to diseases including 'neuron-degenerative disease'.

Lack of Ipsis Verbis Support

The specification is void of literal support for 'lactated Ringer's intravenous polyalklene glycol'. The specification is void of literal support for 'at least about 0.01 ng/ml and up to about 60 ug per 300 microliter'. The specification is void of literal support for the word 'neuron'.

Lack of Implicit or Inherent Support

Section 2163 of the MPEP states: 'While there is no in haec verba requirement, newly added claim limitations must be supported in the specification through express, implicit, or inherent disclosure'.

The specification refers to Ringer's intravenous vehicles. However, such disclosure does not lead one to 'lactated Ringer's intravenous polyalklene glycol' of claim 136.

The specification (figures 6-7) shows specific concentrations of thymosin beta 4 used in a particular assay. However, there is no support for 'about' 0.01 ng/ml or 'about' 60 ug per 300 microliter. Further, it appears that disparate sections of the specification have been used to come up with the ranges recited in the claims. It is noted that claims 173-176 depend from claims 1,13,23,53 respectively. However, one would not have necessarily recognized the use of the instantly claimed ranges for applications of claims 1,13,23,53.

The specification does not use the word 'neuron' thus one would recognize that 'neuron-degenerative disease' of claims 185-186 are not contemplated.

For at least these reasons, one would not conclude that the specification provides adequate support for Claims 136,173-176,185-186.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 1-3,5-7,11,13-14,16-18,22-29,33-36,38-39,53-55,57-59,61,133-136,173-176,183-186 are rejected under 35 U.S.C. 102(e) as being anticipated by Mann (US 6,030,948). It is noted that the 102(e) date for Mann is Dec. 19, 1997 based on MPEP section 706.02(f)(1) section III for a patent that is not from an international application and in which there is no international application in the continuity chain.

Mann teach a composition (claim 1, Tables 13-16) containing thymosin fraction 5. The thymosin fraction 5 includes both thymosin β4 (which comprises the sequence LKKTET) and thymosin α1 (which itself can augment the wound healing process – see page 11 of specification of the current invention thus meeting the limitation of claim 3 for example).

Claim 8 of Mann also teaches combinations of thymosin α1 and thymosin β4 thus meeting the composition limitations recited in claims 1-3,5-7,11,13-14,16-18,22-29,33-36,38-39,53-55,57-59,61,133-136,173-176,183-186 of the instant invention.

Mann teach a method of applying this composition to the scalp (claim 8). Prior to application to the scalp, an acid peel (i.e. chemical peel) solution is applied to the scalp and then removed. As such there is a reasonable basis that the removal of an acid peel solution would result in the removal of an outer layer of the skin and result in abrasion/damage/lesions/wounds on the skin. Mann teach that the composition can be applied topically as a lotion or gel (column 3 lines 52-63, thus meeting the limitations of claims 5-7 for example) and can be used for males or females (Tables 13-16). Since the composition is applied to the skin it is applied to a tissue and specifically to epithelial cells thus meeting the patient population of claims 1-3,5-7,11,13-14,16-18,22-29,33-36,38-39,53-55,57-59,61,133-136,173-176,183-186 of the instant invention.

Section 2111.02 of the MPEP states:

> During examination, statements in the preamble reciting the purpose or intended use of the claimed invention must be evaluated to determine whether the recited purpose or intended use results in a structural difference (or, in the case of process claims, manipulative difference) between the claimed invention and the prior art. If so, the recitation serves to limit the claim. See, e.g., In re Otto, 312 F.2d 937, 938, 136 USPQ 458, 459 (CCPA 1963)

In the instant case, limitations such as promoting migration (claim 53) do not result in a manipulative difference and do not serve to limit the claims.

Although unclear (see 112 2nd) the terms 'isoform' and 'conservative variant' are given the broadest reasonable interpretation. It is noted that certain claims state that 'at least one of a hydrophobic amino acid residues is replaced for another hydrophobic amino acid residue in said amino acid sequence or a polar amino acid residue is replaced for another polar amino acid residue'. However, the claims are not limited to those changes (note the use of the phrase 'at least'). It is noted that claim 136 recites 'an excipient or a composition'. As such, the claim is not limited to the recited compositions as the claim is open to an excipient. Further, Mann teach

alcohols such as phenoxyethanol (table 14). It is noted that claims 173-175 recite ranges which include up to about 60 ug per 300ul (i.e. 200000 ng/ml). In the instant case, the Office has no facility to test the concentration of the thmyosin beta 4 in the thymosin fraction as shown in the tables of Mann. Please note, since the Office does not have the facilities for examining and comparing Applicants' composition with the composition of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art. *See In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald*, 619 F.2d 67, 205 USPQ 594 (CCPA 1980), and "as a practical matter, the Patent Office is not equipped to manufacture products by the myriad of processes put before it and then obtain prior art products and make physical comparisons therewith." *In re Brown*, 459 F.2d 531, 535, 173 USPQ 685, 688 (CCPA 1972).

Response to Arguments 102e rejection

Since claims were previously rejected under 102 using the Mann reference applicants arguments will be considered to the extent that they apply to the instant rejections.

Applicants argue that a declaration has been filed in which an expert states that the acid peels are used for exfoliation and rid the skin surface of dead cells.

Applicants argue that the declaration state that the acids accelerate shedding and loosening of skin and one cannot hurt dead cells.

Applicants argue that the declaration state that any person skilled in the art would recognize that surface acting peels do not cause abrasion/damage/lesions/wounds on skin.

Applicants state that acid peels cause surface exfoliation by reducing cellular cohesiveness and/or by denaturing proteins.

Applicant's arguments and affidavit filed 9/17/08 have been fully considered but they are not persuasive.

The declaration under 37 CFR 1.132 filed 9/17/08 is insufficient to overcome the rejection of claims 1-3,5-7,11,13-14,16-18,22-29,33-36,38-39,53-55,57-59,61,133-136,173-176,183-186 based upon a rejection under 35 U.S.C. 102(e) as being anticipated by Mann (US 6,030,948) as set forth in the last Office action.

First, it is noted that 'wound' is not specifically defined in the instant specification. As such, the claims are given the broadest reasonable interpretation in accord with section 2111 of the MPEP. In the instant case, claim 133 is evidence that the term 'wound' represents a genus of wounds that includes, for example, the many different wounds recited in claim 133. It is noted that the active step of claim 23 is contacting tissue and does not expressly recite that the patient have a wound. It is noted that claim 185 refers to 'tissue injury'. It is noted that claim 186 is drawn 'preventing' and as such the patient population is not required to have an injury. In summary, whether or not the patient population of Mann has wounds is moot for particular claims based on the wording used in particular claims.

Section 716.01(c) of the MPEP states:

'In assessing the probative value of an expert opinion, the examiner must consider the nature of the matter sought to be established, the strength of any opposing evidence, the interest of the expert in the outcome of the case, and the presence or absence of factual support for the expert's opinion. Ashland Oil, Inc. v. Delta Resins & Refractories, Inc., 776 F.2d 281, 227 USPQ 657 (Fed. Cir. 1985), cert. denied, 475 U.S. 1017 (1986).'

In the instant case, the expert is of the opinion that that any person skilled in the art would recognize that surface acting peels do not cause abrasion/damage/lesions/wounds on skin. However, specific facts or or data or references to support such a conclusion are not convincingly set forth. It is noted that the declaration refers to Table 10 of Mann. Although the expert asserts and concludes that such composition would have certain properties, no experimental or documentary evidence has been provided.

As quoted above section 716.01(c) of the MPEP states that the interest of the expert in the outcome is a factor to consider. In the instant case, Regenerx Corporate Presentation (retrieved from http://www.regenerx.com/pdf/NCInvestorPresentation_v38.ppt on 4/13/09 34 pages) teach that (page 32) Jo-David Fine, the expert listed in the declaration, is an advisor for the company Regenerx whose founder (page 31-32) is one of the inventors of the instant invention. As such, there is a reasonable basis that the expert has an interest in the outcome.

In view of the foregoing, when all of the evidence is considered, the totality of the rebuttal evidence fails to outweigh the evidence of record.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 186 is rejected under 35 U.S.C. 102(b) as being anticipated by Goldstein et al. (US 5,578,570 as cited in the IDS 2/21/08).

Godlstein teach the administration of thymosin B4 (claim 1 for example) to a mammal.

It is noted that claims 186 is drawn to method of prevention. Since a method of prevention is used on a patient population prior to the onset of the ailment/disorder, any patient population is available for preventative administration. The patient population described by Goldstein includes mammals (claim 1) and therefore meets the patient population of claims 186 of the instant invention. Further, Goldstein teach the active step (administration of of thymosin B4 (claim 1)) of claims 186 of the instant invention.

Although unclear (see 112 2nd) the terms 'isoform' and 'conservative variant' are given the broadest reasonable interpretation. It is noted that certain claims state that 'at least one of a hydrophobic amino acid residues is replaced for another hydrophobic amino acid residue in said amino acid sequence or a polar amino acid residue is replaced for another polar amino acid residue'. However, the claims are not limited to those changes (note the use of the phrase 'at least').

Response to Arguments 102b rejection

Since claims were previously rejected under 102b, applicants arguments will be considered to the extent that they apply to the instant rejections.

Applicants argue that Goldstein does not teach prevention.

Applicant's arguments filed 9/17/08 have been fully considered but they are not persuasive.

Although applicants argue that Goldstein does not teach prevention, it is noted that claims 186 is drawn to method of prevention. Since a method of prevention is used on a patient population prior to the onset of the ailment/disorder, any patient population is available for

preventative administration. The patient population described by Goldstein includes mammals (claim 1) and therefore meets the patient population of claims 186 of the instant invention. Further, Goldstein teach the active step (administration of thymosin B4 (claim 1)) of claim 186 of the instant invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-3,5-8,11,13-14,16-19,22-29,33-36,38-39,53-55,57-61,133-136,173-176,183-186 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mann (US 6,030,948).

As discussed above, Mann teach methods of administering a composition comprising thymosin β4. Mann does not expressly teach the use of a recombinant or synthetic TB4 as in claims 8,19; the in vitro use as in claim 60; the use of sterile water as in claim 136.

Mann does expressly teach the use of thymosin beta 4 (claim 8). Since recombinant expression and purification of proteins is well-known in the art one of skill in the art would have been motivated to substitute the thymus purified peptide as taught by Mann with a recombinant or synthetic peptide while maintaining an expectation of predictable results since the primary sequence of the protein is retained. Thus Mann obviates claims 8,19 of the instant invention.

Mann expressly teach the use of a vehicle (Tables 14-16) for the compositions. Since maintaining a pure, uncontaminated product is a goal one would be motivated to use sterile water as a specific vehicle while maintaining an expectation of predictable results since the same active ingredients are used. Thus Mann obviates claim 136 of the instant invention

Mann recognizes the use of in vitro experiments (Table 1). It would be obvious to one of skill in the art to determine if similar results could be obtained *in vitro* so that experimental results could be achieved in a more cost effective manner in a laboratory setting instead of requiring human subjects. Thus Mann obviates claim 60 of the instant invention.

From the teachings of the reference, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the reference, especially in the absence of evidence to the contrary.

Although unclear (see 112 2nd) the terms 'isoform' and 'conservative variant' are given the broadest reasonable interpretation. It is noted that certain claims state that 'at least one of a hydrophobic amino acid residues is replaced for another hydrophobic amino acid residue in said amino acid sequence or a polar amino acid residue is replaced for another polar amino acid residue'. However, the claims are not limited to those changes (note the use of the phrase 'at least').

Section 2111.02 of the MPEP states:

> During examination, statements in the preamble reciting the purpose or intended use of the claimed invention must be evaluated to determine whether the recited purpose or intended use results in a structural difference (or, in the case of process claims, manipulative difference) between the claimed invention and the prior art. If so, the recitation serves to limit the claim. See, e.g., In re Otto, 312 F.2d 937, 938, 136 USPQ 458, 459 (CCPA 1963)

In the instant case, limitations such as promoting migration (claim 53) do not result in a manipulative difference and do not serve to limit the claims.

Claims 1-2,5-8,11,13,16-19,23-28,33-35,38-39,53-55,57-61,133-136,173-176,183-186 are rejected under 35 U.S.C. 103(a) as being unpatentable over Malinda et al (Faseb Journal 1997 cited in IDS 5/25/01) and Baumann et al 1997 (from 'Thymic peptides in preclinical and clinical medicine: an update:proceedings of the 2nd international thymus symposium' editor HR Maurer, pages 13-17) and Biotech Patent News (Dec 1 1997 1 page).

Malinda teach that Thymosin beta 4 (TB4) acts as a chemoattractant for endothelial cells (abstract). Malinda teach that in vitro wound closure is more rapid in the presence of TB4 (page 477). Malinda teach that cell migration is enhanced by TB4 (page 478). Malinda teach that TB4 is important in angiogenesis and that the formation of blood vessels is an important part of

wound healing (page 480). Malinda teach that others report that TB4 could play a major role in would healing (page 480).

Malinda does not expressly teach administration of TB4 to patients in need of wound healing.

Malinda teach that TB4 is important in angiogenesis and that the formation of blood vessels is an important part of wound healing (page 480). Malinda teach that others report that TB4 could play a major role in would healing (page 480). Malinda recognizes the use of in vivo experiments (abstract). Since Malinda teach positive results for the in vitro studies (see wound closure model page 477) one would be motivated to use the method in vivo.

Further, Baumann (Table II page 21) also teach that TB4 leads to an increase in wound healing in vitro.

Further, Biotech Patent News teach that investigators will use thymosin beta 4 (last paragraph) in a wound healing study.

Taken together, the prior art clearly recognizes the use of TB4 for wound healing. Although the references do not expressly teach in a single embodiment the use for patients in need thereof one would be motivated to use TB4 in patients based on the promising in vitro results. One would have a reasonable expectation of success based on the in vitro results reported in the prior art.

Since Biotech patent news teach the use in wound healing studies one would be motivated to use TB4 specifically for those with wounds. Since Malinda teach the use of a scratch wound closure assay (page 475) one would be motivated to use TB4 in vivo for skin

wounds. In order to use the TB4 for skin wounds one would be motivated to prepare the TB4 with an appropriate excipient such as water and an appropriate form such as a lotion for administration to the skin. Since in vitro models are used as a precursor to use in humans one would be motivated to use the methods on humans and apply TB4 to skin cells including epithelial cells (see page 474 of Malinda) based on the promising in vitro results. Although Malinda does not recite the source of the protein one would recognize that recombinant or synthetic production is a well known method in the art for production of peptides. Thus taken together the references obviate the use of a specific agent (thymosin beta 4) which reads on the polypeptide as recited in the instant claims; the references motivate a specific use (wound healing) which motivates specific excipients, forms, and locations of administration as recited in the instant claims.

Further, it would have been obvious to one skilled in the art at the time of invention to determine all optimum and operable conditions (e.g.doses), because such conditions are art-recognized result-effective variables that are routinely determined and optimized in the art through routine experimentation. ("[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). *See* MPEP § 2144.05).

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at

the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Although unclear (see 112 2nd) the terms 'isoform' and 'conservative variant' are given the broadest reasonable interpretation. It is noted that certain claims state that 'at least one of a hydrophobic amino acid residues is replaced for another hydrophobic amino acid residue in said amino acid sequence or a polar amino acid residue is replaced for another polar amino acid residue'. However, the claims are not limited to those changes (note the use of the phrase 'at least').

Section 2111.02 of the MPEP states:

> During examination, statements in the preamble reciting the purpose or intended use of the claimed invention must be evaluated to determine whether the recited purpose or intended use results in a structural difference (or, in the case of process claims, manipulative difference) between the claimed invention and the prior art. If so, the recitation serves to limit the claim. See, e.g., In re Otto, 312 F.2d 937, 938, 136 USPQ 458, 459 (CCPA 1963)

In the instant case, limitations such as promoting migration (claim 53) do not result in a manipulative difference and do not serve to limit the claims.

Claims 1-8,11,13-19,22-30,33-36,38-39,53-55,57-61,133-136,173-176,183-186 are rejected under 35 U.S.C. 103(a) as being unpatentable over Malinda et al (Faseb Journal 1997 cited in IDS 5/25/01) and Baumann et al 1997 (from 'Thymic peptides in preclinical and clinical medicine: an update:proceedings of the 2nd international thymus symposium' editor HR Maurer, pages 13-17) and Biotech Patent News (Dec 1 1997 1 page) and Puolakkainen et al (Journal of Surgical Research v58 1995 pages 321-329).

As discussed above, Malinda, Baumann, and Biotech Patent News obviate the use of TB4 for wound healing.

However, the references do not expressly teach in a single embodiment the use of a further agent (as recited in claims 3,14,22,29,36) or the use of TGF-beta (claims 4,15,30).

Puolakkainen recognize what is well-known in the art, that TGF-beta is known to enhance wound healing (title, page 325 discussion). Puolakkainen also recognize the optimization of the administration mode and dose and teach toward topical administration (abstract and throughout). One would be motivated to use the teachings of Puolakkainen along with the other references since the references are drawn to methods of wound healing.

In the instant case, the claimed elements (thymosin beta 4, TGF-beta) were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention. Taken together the references meet the limitations of the instant claims. One would have a reasonable expectation of success since both references teach agents for wound healing.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Although unclear (see 112 2nd) the terms 'isoform' and 'conservative variant' are given the broadest reasonable interpretation. It is noted that certain claims state that 'at least one of a hydrophobic amino acid residues is replaced for another hydrophobic amino acid residue in said amino acid sequence of a polar amino acid residue is replaced for another polar amino acid residue'. However, the claims are not limited to those changes (note that use of the phrase 'at least').

Section 2111.02 of the MPEP states:

> During examination, statements in the preamble reciting the purpose or intended use of the claimed invention must be evaluated to determine whether the recited purpose or intended use results in a structural difference (or, in the case of process claims, manipulative difference) between the claimed invention and the prior art. If so, the recitation serves to limit the claim. See, e.g., In re Otto, 312 F.2d 937, 938, 136 USPQ 458, 459 (CCPA 1963)

In the instant case, limitations such as promoting migration (claim 53) do not result in a manipulative difference and do not serve to limit the claims.

Response to Arguments 103 rejection

Since claims were previously rejected under 103, applicants arguments will be considered to the extent that they apply to the instant rejections.

Applicants set forth no specific arguments directed towards the 103 rejection other than the declaration.

Applicant's arguments and affidavit filed 9/17/08 have been fully considered but they are not persuasive.

The declaration under 37 CFR 1.132 filed 9/17/08 is insufficient to overcome the rejection of claims 1-3,5-7,11,13-14,16-18,22-29,33-36,38-39,53-55,57-59,61,133-136,173-176,183-186 based upon a rejection under 35 U.S.C. 102(e) as being anticipated by Mann (US 6,030,948) as set forth in the last Office action.

First, it is noted that 'wound' is not specifically defined in the instant specification. As such, the claims are given the broadest reasonable interpretation in accord with section 2111 of the MPEP. In the instant case, claim 133 is evidence that the term 'wound' represents a genus of wounds that includes, for example, the many different wounds recited in claim 133. It is noted that the active step of claim 23 is contacting tissue and does not expressly recite that the patient have a wound. It is noted that claim 185 refers to 'tissue injury'. It is noted that claim 186 is drawn 'preventing' and as such the patient population is not required to have an injury. In summary, whether or not the patient population of Mann has wounds is moot for particular claims based on the wording used in particular claims.

Section 716.01(c) of the MPEP states:

'In assessing the probative value of an expert opinion, the examiner must consider the nature of the matter sought to be established, the strength of any opposing evidence, the interest of the expert in the outcome of the case, and the presence or absence of factual support for the expert's opinion. Ashland Oil, Inc. v. Delta Resins & Refractories, Inc., 776 F.2d 281, 227 USPQ 657 (Fed. Cir. 1985), cert. denied, 475 U.S. 1017 (1986).'

In the instant case, the expert is of the opinion that that any person skilled in the art would recognize that surface acting peels do not cause abrasion/damage/lesions/wounds on skin.

However, specific facts or or data or references to support such a conclusion are not convincingly set forth. It is noted that the declaration refers to Table 10 of Mann. Although the expert asserts and concludes that such composition would have certain properties, no experimental or documentary evidence has been provided.

As quoted above section 716.01(c) of the MPEP states that the interest of the expert in the outcome is a factor to consider. In the instant case, Regenerx Corporate Presentation (retrieved from http://www.regenerx.com/pdf/NCInvestorPresentation_v38.ppt on 4/13/09 34 pages) teach that (page 32) Jo-David Fine, the expert listed in the declaration, is an advisor for the company Regenerx whose founder (page 31-32) is one of the inventors of the instant invention. As such, there is a reasonable basis that the expert has an interest in the outcome.

In view of the foregoing, when all of the evidence is considered, the totality of the rebuttal evidence fails to outweigh the evidence of record.

Double Patenting

The terminal disclaimer filed on 9/17/08 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of US 7,268,118 has been reviewed and is accepted. The terminal disclaimer has been recorded.

The terminal disclaimer filed on 9/17/08 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of any patent granted on 11/284,430 has been reviewed and is accepted. The terminal disclaimer has been recorded.

It is noted that 10/714,405 has been abandoned.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-8,11,13-19,22-30,33-36,38-39,53-55,57-61,133-136,173-176,183-186 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 7-16,29-47 of copending Application No. 11/284,408 ('408). Although the conflicting claims are not identical, they are not patentably distinct from each other because the '408 application teaches methods of administering compositions to the skin comprising thymosin beta four (for example, claim 7), transforming growth factor (claim 8), for topical treatment (for example, claim 7). '408 teach the administration to skin specifically damaged skin (claim 29) and specifically to epithethial tissue (claim 38). '408 teach doses (claim 38,29) that meet the limitations of the instant claims.

Further, it is noted that claim 186 is drawn to methods of prevention. Since a method of prevention is used on a patient population prior to the onset of the ailment/disorder, any patient population is available for preventative administration.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1-3,5-7,11,13-14,16-18,22-29,33-36,38-39,53-55,57-59,61,133-136,173-176,183-186 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 13-23,26 of copending Application No. 11/917,869 ('869). Although the conflicting claims are not identical, they are not patentably distinct from each other because the '869 application teaches methods of administering compositions to the skin comprising thymosin beta four isoform or LKKTET (for example, claim 13,21), and specific doses (claim 23) as in the instant claims.

Further, it is noted that claim 186 is drawn to methods of prevention. Since a method of prevention is used on a patient population prior to the onset of the ailment/disorder, any patient population is available for preventative administration.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1-3,5-7,11,13-14,16-18,22-29,33-36,38-39,53-55,57-59,61,133-136,173-176,183-186 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 21-32 of copending Application No. 11/715,997 ('997). Although the conflicting claims are not identical, they are not patentably distinct from each other

because the '997 application teaches methods of administering compositions to the skin comprising thymosin beta four or LKKTET (for example, claim 21), and specific doses (claim 27) as in the instant claims.

Further, it is noted that claim 186 is drawn to methods of prevention. Since a method of prevention is used on a patient population prior to the onset of the ailment/disorder, any patient population is available for preventative administration.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1-3,5-7,11,13-14,16-18,22-29,33-36,38-39,53-55,57-59,61,133-136,173-176,183-186 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-25 of copending Application No. 12/444,331 ('331). Although the conflicting claims are not identical, they are not patentably distinct from each other because the '331 application teaches methods of administering compositions to the skin comprising thymosin beta four or LKKTET (for example, claim 1), and specific doses (claim 7) as in the instant claims.

Further, it is noted that claim 186 is drawn to methods of prevention. Since a method of prevention is used on a patient population prior to the onset of the ailment/disorder, any patient population is available for preventative administration.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP Chapter 2300). Commonly assigned 11/715,997 and 12/444,331; discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications pending on or after December 10, 2004.

Response to Arguments double patenting

Applicants arguments will be considered to the extent that they apply to the instant rejections.

Applicants argue that 11/284,408 and 11/917,869 are not commonly owned.

Applicants argue that 11/917,869 is drawn to administration of a quaternary ammonium salt.

Applicant's arguments filed 9/17/08 have been fully considered but they are not persuasive.

Although Applicants argue that 11/284,408 and 11/917,869 are not commonly owned, there is a common inventor (Allan Goldstein for example). MPEP section 804 Chart I-B shows that a double patenting rejection is appropriate when there is at least one common inventor.

Although applicants argue that 11/917,869 is drawn to administration of a quaternary ammonium salt, 11/917,869 claim 13 is drawn to administration of a peptide comprising amino acid sequence LKKTET (or an isoform claim 21) as in the instant invention. Whether or not additional steps or components are present in '869 is moot since '869 reads on the instant claims.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to RONALD T. NIEBAUER whose telephone number is (571)270-3059. The examiner can normally be reached on Monday-Thursday, 7:30am-5:00pm, alt. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Anish Gupta/
Primary Examiner, Art Unit 1654

/Ronald T Niebauer/
Examiner, Art Unit 1654